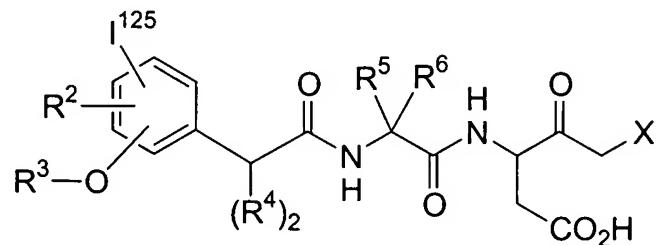


**Amendments to the Claims:**

This listing of claims replaces all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (original) A compound represented by Formula I:



I

or a salt, ester or hydrate thereof, wherein:

$\text{X}$  is halo, or

$\text{X}$  is  $-\text{O}-\text{W}-\text{Z}$ , wherein  $\text{W}$  is a bond,  $-\text{CH}_2-$ ,  $-\text{C}(\text{O})-$  or  $-\text{C}(\text{O})\text{CH}_2-$ ;

$\text{Z}$  is selected from the group consisting of:

- (1) H,
- (2) C<sub>1-11</sub>alkyl,
- (3) C<sub>3-11</sub>cycloalkyl or a benzofused analog thereof,
- (4) phenyl or naphthyl, and
- (5) HET<sup>1</sup>, wherein HET<sup>1</sup> represents a 5- to 10-membered mono- or bicyclic, aromatic or non-aromatic ring, or a benzofused analog thereof, containing 1-3 heteroatoms selected from O, S and N,

groups (2), (3) and (5) above are optionally substituted with 1-2 oxo groups,

groups (2) – (5) above are further optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo
- (b) nitro,
- (c) hydroxy,
- (d) C<sub>1-4</sub>alkyl,
- (e) C<sub>1-4</sub>alkoxy,
- (f) C<sub>1-4</sub>alkylthio,
- (g) C<sub>3-6</sub>cycloalkyl,
- (h) phenyl or naphthyl,
- (i) phenoxy,
- (j) benzyl,
- (k) benzyloxy, and
- (l) a 5 or 6-membered aromatic or non-aromatic ring containing from 1-3 heteroatoms selected from O, S and N,

groups (d)-(g) above are optionally substituted with oxo and 1-3 substituents independently selected from halo and C<sub>1-4</sub>alkoxy,

groups (h) – (l) above are optionally substituted with 1-3 substituents independently selected from halo and C<sub>1-4</sub>alkyl, and

group (4) is further optionally substituted up to its maximum with halo groups;

R<sup>2</sup> is selected from the group consisting of:

- (1) H,
- (2) halo,
- (3) hydroxy,
- (4) nitro,
- (5) cyano,
- (6) C<sub>1-10</sub>alkyl, C<sub>3-10</sub>cycloalkyl, C<sub>1-10</sub>alkoxy, -S(O)0-2C<sub>1-10</sub>alkyl or -NHC<sub>1-10</sub>alkyl, each optionally substituted with 1-2 oxo or carboxy groups and further optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo,
- (b) hydroxy
- (c) cyano,
- (d) C<sub>1-4</sub>alkoxy,
- (e) -NHR<sup>7</sup>, wherein R<sup>7</sup> is independently H or C<sub>1-5</sub>alkyl,
- (f) -S(O)0-2C<sub>1-4</sub>alkyl, and
- (g) HET<sup>2</sup>, wherein HET<sup>2</sup> represents a 5- to 7-membered aromatic or non-aromatic ring containing 1-4 heteroatoms selected from O, S and NR<sup>8</sup>, wherein R<sup>8</sup> is independently H or C<sub>1-5</sub>alkyl, said HET<sup>2</sup> being optionally substituted with oxo and further optionally substituted with 1-2 substituents independently selected from halo and C<sub>1-4</sub>alkyl, said C<sub>1-4</sub>alkyl being optionally substituted with 1-3 halo groups,

(7) phenoxy or -S(O)0-2phenyl,

(8) benzyloxy or -S(O)0-2benzyl,

(9) benzoyl,

(10) phenyl or naphthyl,

(11) -O-HET<sup>2</sup> or -S-HET<sup>2</sup>, said HET<sup>2</sup> being optionally substituted with oxo and further optionally substituted as defined below, and

(12) HET<sup>3</sup>, wherein HET<sup>3</sup> is a 5- or 6-membered aromatic or non-aromatic ring, or a benzofused analog thereof, containing from 1 to 4 heteroatoms selected from O, S and N, said HET<sup>3</sup> being optionally substituted with oxo and further optionally substituted as defined below,

groups (7) - (12) above are each optionally substituted with 1-2 substituents independently selected from the group consisting of: halo, cyano, C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy, said C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy being optionally substituted with 1-3 halo groups;

R<sup>3</sup> is phenyl or C<sub>1-10</sub>alkyl, said C<sub>1-10</sub>alkyl optionally substituted with 1-2 oxo or carboxy groups and further optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo,
- (b) hydroxy
- (c) cyano,
- (d) C<sub>1-4</sub>alkoxy,

(e)  $-\text{NHR}^7$ , wherein  $\text{R}^7$  is independently H or C<sub>1-5</sub>alkyl,  
(f)  $-\text{S}(\text{O})_0\text{--2C}_1\text{-4alkyl}$ , and  
(g) HET<sup>2</sup>, wherein HET<sup>2</sup> represents a 5- to 7-membered aromatic or non-aromatic ring containing 1-4 heteroatoms selected from O, S and NR<sup>8</sup>, wherein R<sup>8</sup> is independently H or C<sub>1-5</sub>alkyl, said HET<sup>2</sup> being optionally substituted with oxo and further optionally substituted with 1-2 substituents independently selected from halo or C<sub>1-4</sub>alkyl, said C<sub>1-4</sub>alkyl being optionally substituted with 1-3 halo groups,

each R<sup>4</sup> is independently selected from the group consisting of: H, halo, hydroxy, C<sub>1-6</sub>alkyl and C<sub>1-4</sub>alkoxy, said C<sub>1-6</sub>alkyl and C<sub>1-4</sub>alkoxy being optionally substituted with oxo and further optionally substituted with 1-3 halo groups; and

R<sup>5</sup> is selected from the group consisting of: H, phenyl, naphthyl, C<sub>1-6</sub>alkyl optionally substituted with OR<sup>12</sup> and 1-3 halo groups, and C<sub>5-7</sub> cycloalkyl optionally containing one heteroatom selected from O, S and NR<sup>13</sup>,

wherein R<sup>12</sup> is selected from the group consisting of: H, C<sub>1-5</sub>alkyl optionally substituted with 1-3 halo groups, and benzyl optionally substituted with 1-3 substituents independently selected from halo, C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy, and

R<sup>13</sup> is H or C<sub>1-4</sub>alkyl optionally substituted with 1-3 halo groups; and

R<sup>6</sup> represents H;

or in the alternative, R<sup>5</sup> and R<sup>6</sup> are taken in combination and represent a ring of 4-7 members, said ring optionally containing one heteroatom selected from O, S and NR<sup>13</sup>.

2. (original) The compound according to Claim 1 wherein X is halo.
3. (original) The compound according to Claim 1 wherein X is  $-\text{O}\text{--W}\text{--Z}$ .
4. (original) The compound according to Claim 3 wherein Z is selected from the group consisting of:

- (1) C<sub>1-11</sub>alkyl,
- (2) C<sub>3-11</sub>cycloalkyl or a benzofused analog thereof, and
- (3) phenyl or naphthyl,

wherein groups (1) – (3) above are optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo
- (b) nitro,
- (c) hydroxy,
- (d) C<sub>1-4</sub>alkyl,
- (e) C<sub>1-4</sub>alkoxy,
- (f) C<sub>1-4</sub>alkylthio,
- (g) C<sub>3-6</sub>cycloalkyl,
- (h) phenyl or naphthyl,
- (i) phenoxy,
- (j) benzyl and
- (k) benzyloxy.

5. (original) The compound according to Claim 1 wherein R<sup>3</sup> is methyl.

6. (original) The compound according to claim 1 wherein R<sup>2</sup> and each R<sup>4</sup> are hydrogen.

7. (original) The compound according to claim 1 wherein R<sup>5</sup> is selected from the group consisting of: C<sub>1-6</sub>alkyl, phenyl and naphthyl.

8. (original) The compound according to claim 1 wherein:

X is halo or –O-W-Z;

W is a bond, -CH<sub>2</sub>-, -C(O)- or -C(O)CH<sub>2</sub>-;

Z is selected from the group consisting of:

- (1) C<sub>1</sub>-6alkyl, optionally substituted with 1-3 halo groups,
- (2) C<sub>3</sub>-11cycloalkyl or a benzofused analog thereof, and
- (3) phenyl or naphthyl, optionally substituted with 1-3 groups independently selected from halo or C<sub>1</sub>-4alkyl,

R<sup>3</sup> is methyl, ethyl or phenyl;

R<sup>2</sup> and each R<sup>4</sup> are hydrogen;

R<sup>5</sup> is selected from the group consisting of: C<sub>1</sub>-6alkyl, ~~C<sub>5</sub>-7cycloalkyl~~ C<sub>5</sub>-7cycloalkyl, phenyl and naphthyl; and

R<sup>6</sup> is hydrogen.

9 to 11. (canceled)

12. (withdrawn) A method for detecting active caspase-3 in cells or tissues of a mammal comprising contacting said cells or tissues with a compound of Claim 1 and detecting active caspase-3.

13. (canceled)

14. (withdrawn) A method for determining the caspase-3 active site occupancy of a sample reversible caspase-3 inhibitor in an animal model of cellular injury comprising:

- 1) administering to said animal said sample reversible caspase-3 inhibitor;
- 2) euthanizing said animal and extracting said injured cells;
- 3) contacting said injured cells *ex vivo* with a compound according to Claim 1;
- 4) detecting the amount of said compound to determine the number of caspase-3 free active sites; and

5) comparing said number of caspase-3 free active sites to the total measure of active caspases to determine the caspase-3 active site occupancy.

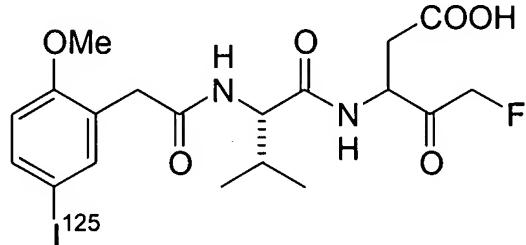
15. (withdrawn) A method for determining the caspase-3 active site occupancy of a sample reversible caspase-3 inhibitor in a cell culture comprising:

- 1) contacting said cell culture with a sample reversible caspase-3 inhibitor;
- 2) contacting said cell culture with a compound according to Claim 1;
- 3) detecting the amount of said compound to determine the number of caspase-3 free active sites; and
- 4) comparing said number of caspase-3 free active sites to the total measure of active caspases to determine the caspase-3 active site occupancy.

16. (withdrawn) A kit for detecting active caspase-3 in cells or tissues of a mammal comprising a compound of Claim 1.

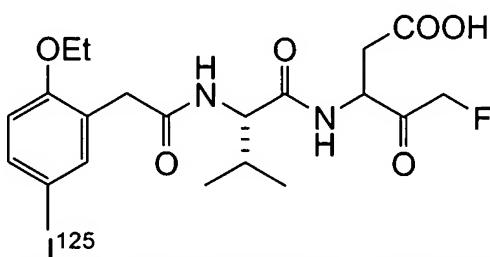
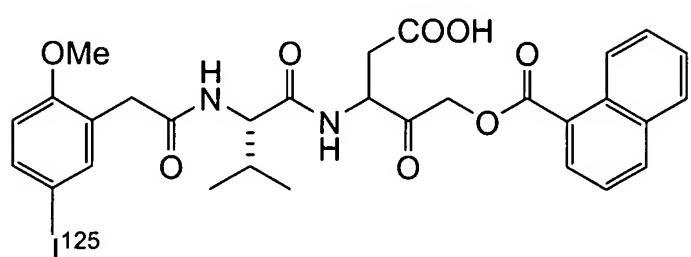
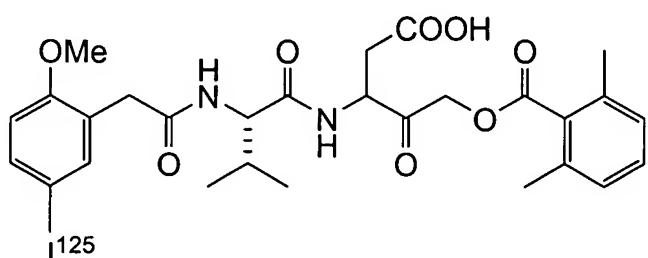
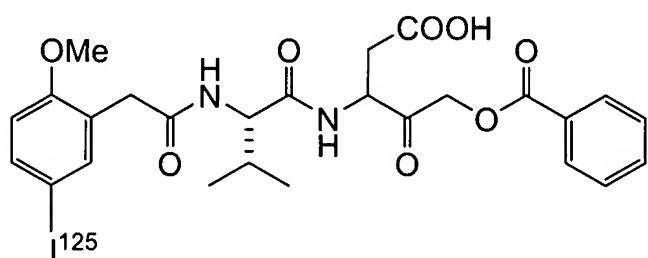
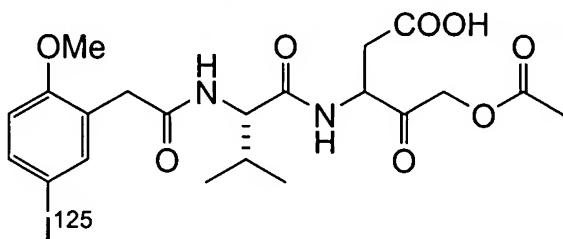
17. (canceled)

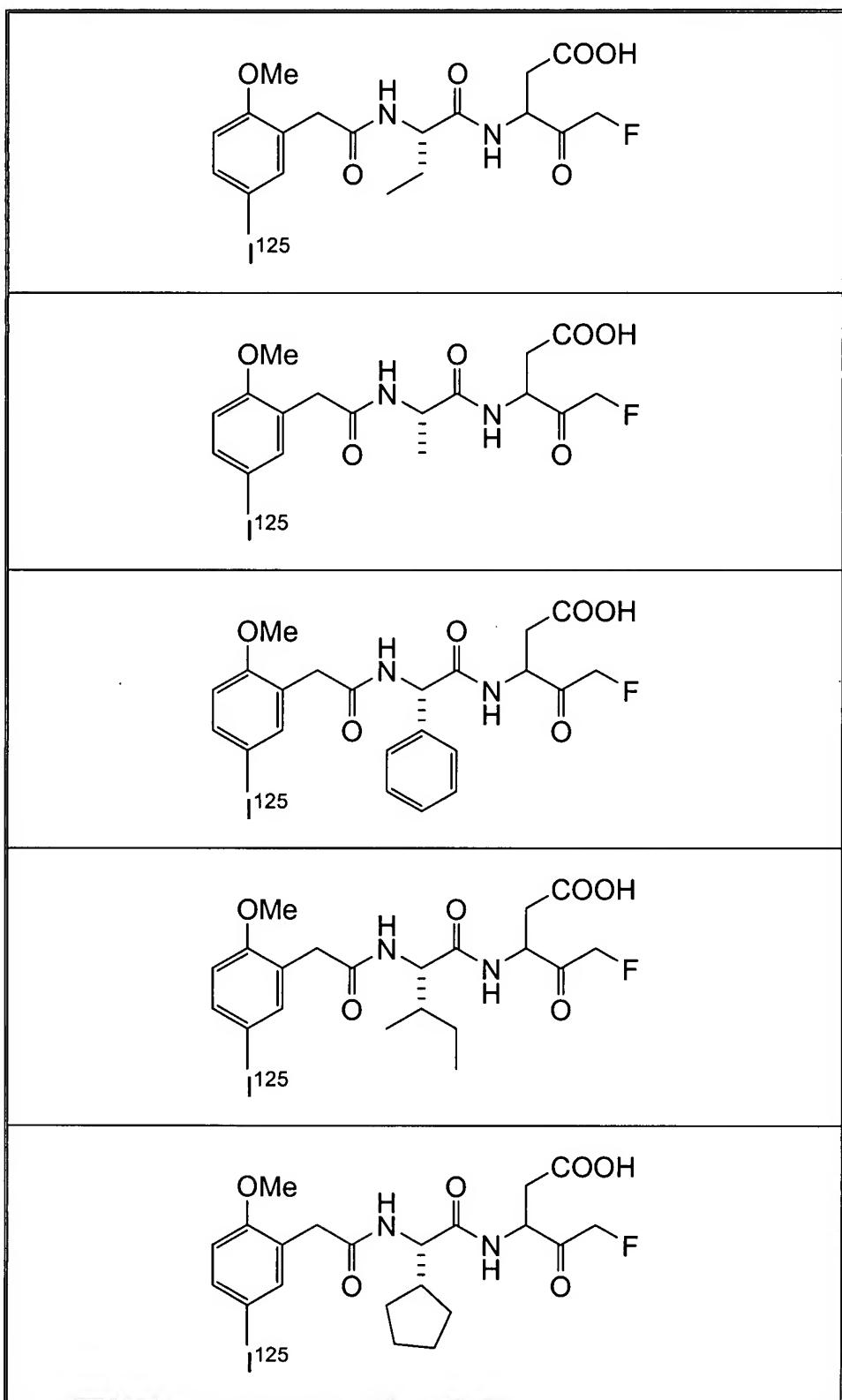
18. (original) The compound according to Claim 1 which is

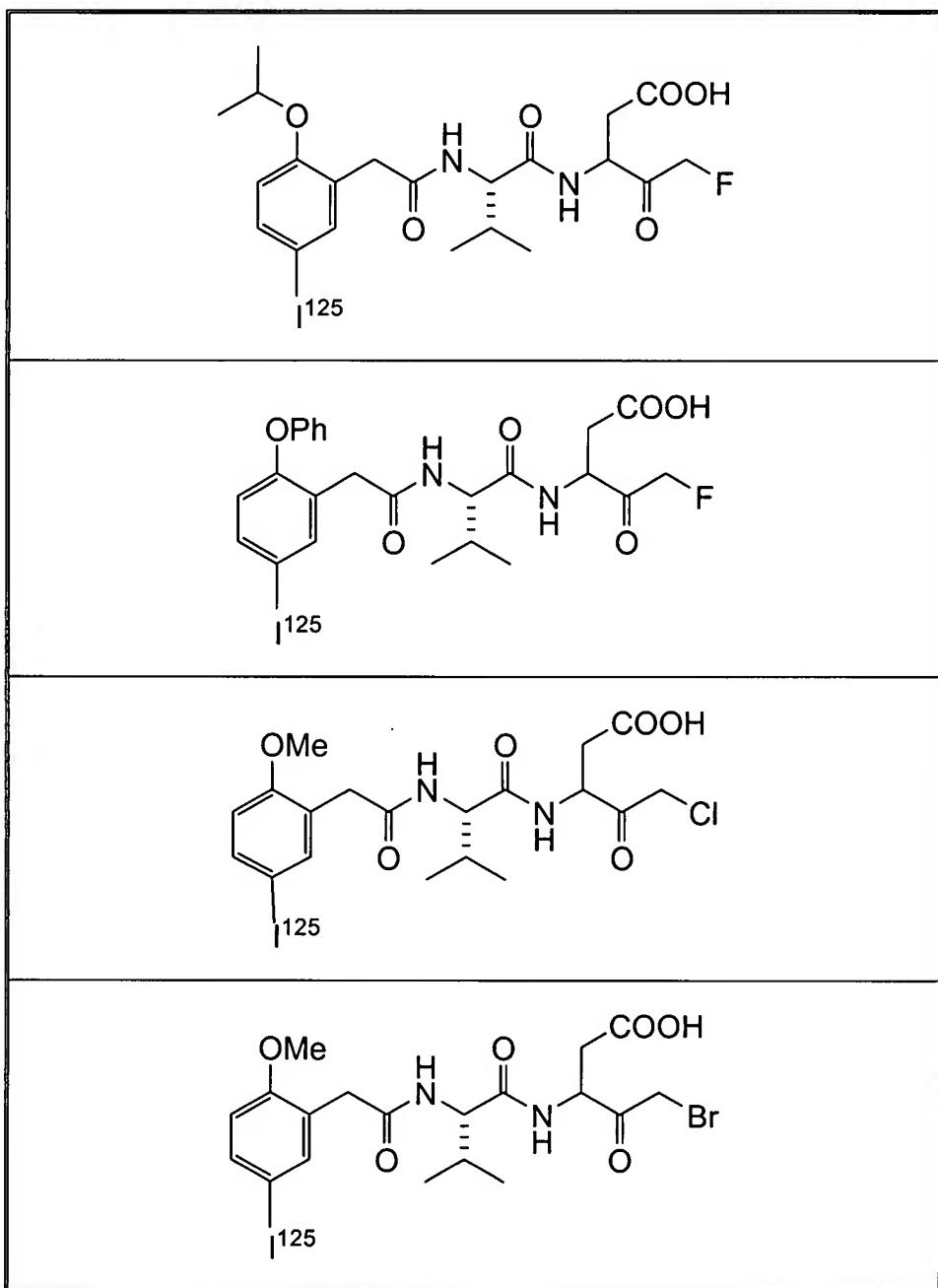


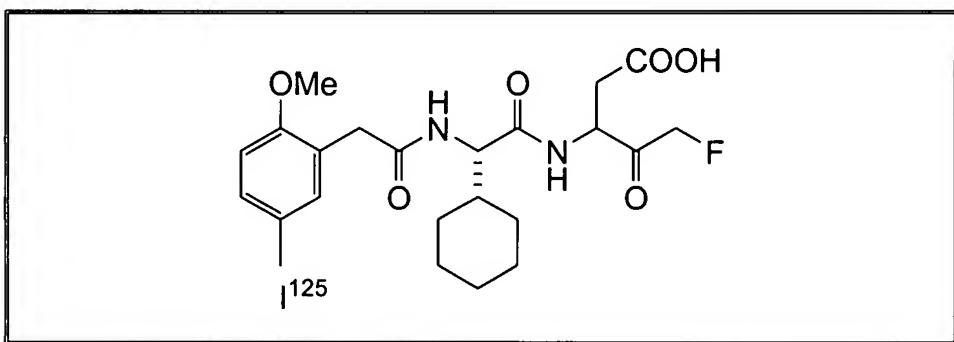
or a salt, ester or hydrate thereof.

19. (original) A compound according to Claim 1 which is selected from the following table:









or a salt, ester or hydrate of any of the above.

20. (withdrawn) A compound of any one of claims 1 to ~~11~~ 8, 18 or 19 for use in detecting active caspase-3 in cells or tissues of a mammal.

21. (withdrawn) A compound of any one of claims 1 to ~~11~~ 8, 18 or 19 for use in determining the caspase-3 active site occupancy of a sample reversible caspase-3 inhibitor in an animal model of cellular injury.